

B2 cont.  
transgenic plant, which transgenic plant cell or plant is transformed or transfected with a recombinant expression construct comprising a nucleotide sequence encoding the lysosomal enzyme and a promoter that regulates expression of the nucleotide sequence so that the lysosomal enzyme is expressed by the transgenic plant cell or plant;

wherein the transgenic plant or plant cell is transformed or transfected with the recombinant expression construct, and the modified lysosomal enzyme has the amino acid sequence of the lysosomal enzyme with one or several amino acid substitutions, additions and/or deletions, and the organ is a leaf, stem, root, flower, fruit or seed].

B3  
77 (twice amended) The method according to claim ~~51~~<sup>66</sup> [1], in which the modified lysosomal enzyme comprises a signal peptide or detectable marker peptide [fused to] at the amino or carboxyl terminal of the modified lysosomal enzyme.

85 (amended) The method according to claim 1 [any of claims 1, 4 and 7], in which the lysosomal enzyme [or modified lysosomal enzyme] is a human or animal lysosomal enzyme [or modified human lysosomal enzyme].

97 (amended) The method according to claim [8] ~~67~~<sup>76</sup>, in which the [human] lysosomal enzyme [or modified human lysosomal enzyme] is a human glucocerebrosidase[, modified glucocerebrosidase,] or human  $\alpha$ -L-iduronidase [or modified  $\alpha$ -L-iduronidase].

B4  
109 (amended) A recombinant expression construct comprising a nucleotide sequence encoding a lysosomal enzyme [or modified lysosomal enzyme] and a promoter that regulates the expression of the nucleotide sequence in a plant cell[, wherein the modified lysosomal enzyme has the amino acid sequence of the lysosomal enzyme with one or more amino acid substitutions, additions and/or deletions].

B5  
1424 (amended) The recombinant expression construct of claim [10] ~~55~~<sup>23</sup>, in which the modified lysosomal enzyme comprises a signal peptide or detectable marker peptide [fused to] at the amino or carboxyl terminal of the modified lysosomal enzyme.

29  
16. (amended) The recombinant expression construct of claim 10<sup>15</sup> or 13], in which the lysosomal enzyme [or modified lysosomal enzyme] is a human or animal lysosomal enzyme [or modified human lysosomal enzyme].

31  
17. (amended) The recombinant expression construct of claim [16] 30<sup>30</sup> 32, in which the [human] lysosomal enzyme [or modified human lysosomal enzyme] is a human glucocerebrosidase[, modified glucocerebrosidase,] or human  $\alpha$ -L-iduronidase [or modified  $\alpha$ -L-iduronidase].

Sub B6  
32  
18. (amended) A plant transformation vector comprising the recombinant expression construct of claim 10, 11, 14, 16, 17, 23, 25, 27 or 32<sup>28</sup> [16].

33  
20. (amended) A plant [cell, tissue or organ] which [has] is transformed or transfected with the recombinant expression construct of claim 10, 11, 14, 16, 17, 23, 25, 27 or 32<sup>28</sup> [16].

B7  
34  
21. (twice amended) A plant cell, tissue or organ which [has] is transformed or transfected with the recombinant expression construct of claim 10, 11, 14, 16, 17, 23, 25, 27 or 32<sup>28</sup>.

B8  
35  
24. (amended) A plasmid pCT54 having the ATCC accession number 97770 [ ].

36  
25. (twice amended) A transgenic plant or plant cell capable of producing [an enzymatically active] a lysosomal enzyme which is enzymatically active [or modified lysosomal enzyme], which transgenic plant or plant cell [has] is transformed or transfected with a recombinant expression construct comprising a nucleotide sequence encoding a lysosomal enzyme [or modified lysosomal enzyme] and a promoter that regulates expression of the nucleotide sequence in the transgenic plant or plant cell[, wherein the transgenic plant or plant cell is transformed or transfected with the recombinant expression construct, and the modified lysosomal enzyme has the amino acid sequence of the lysosomal enzyme with one or more amino acid substitutions, additions and/or deletions].

89 45  
29. (amended) The transgenic plant or plant cell of claim [25] 58, in which the modified lysosomal enzyme comprises a signal peptide or detectable marker peptide [fused to] at the amino or carboxyl terminal of the modified lysosomal enzyme.

51  
32. (amended) The transgenic plant or plant cell of claim 25 [any of claims 25, 28 and 31], in which the lysosomal enzyme [or modified lysosomal enzyme] is a human or animal lysosomal enzyme [or modified human lysosomal enzyme].

B10 53  
33. (amended) The transgenic plant or plant cell of claim [32] 69, in which the [human] lysosomal enzyme [or modified human lysosomal enzyme] is a human glucocerebrosidase[, modified glucocerebrosidase,] or human  $\alpha$ -L-iduronidase [or modified  $\alpha$ -L-iduronidase].

54  
34. (amended) A leaf, stem, root, flower or seed of the transgenic plant of claim [32] 25, 26, 29, 31, 32, 33, 58, 60 or 73.

55  
36. (amended) A [plant grown from a] seed of plant line hGC X-11, which seed has the ATCC Accession No. 97275.

56  
37. (amended) A [plant grown from a] seed of plant line hGC X-27, which seed has the ATCC Accession No. 97276.

B11 57  
38. (amended) A [plant grown from a] seed of plant line CT40-9, which seed has the ATCC Accession No. 97700.

59  
39. (amended) A lysosomal enzyme [or modified lysosomal enzyme] which is enzymatically active and is produced according to a process comprising:

- [(a) growing a transgenic plant or plant cell which transgenic plant or plant cell has a recombinant expression construct comprising a nucleotide sequence encoding the lysosomal enzyme or modified lysosomal enzyme and a promoter that regulates expression of the nucleotide sequence so that the lysosomal enzyme or modified lysosomal enzyme is expressed by the transgenic plant or plant cell; and

- B11 cont
- (b)] recovering the lysosomal enzyme [or modified lysosomal enzyme] from [the] (i) a transgenic plant cell or (ii) a cell, tissue or organ of [the] a transgenic plant which transgenic plant cell or plant is transformed or transfected with a recombinant expression construct comprising a nucleotide sequence encoding the lysosomal enzyme and a promoter that regulates expression of the nucleotide sequence so that the lysosomal enzyme is expressed by the transgenic plant cell or plant [;

wherein the which transgenic plant or plant cell is transformed or transfected with the recombinant expression construct, and the modified lysosomal enzyme has the amino acid sequence of the lysosomal enzyme with one or more amino acid substitutions, additions and/or deletions, and the organ is a leaf, stem, root, flower, fruit or seed].

60  
40. (twice amended) The lysosomal enzyme [or modified lysosomal enzyme] of claim 39, in which the promoter is an inducible promoter.

61  
41. (amended) The lysosomal enzyme [or modified lysosomal enzyme] of claim 40, in which the inducible promoter comprises SEQ ID NO:5.

B12  
64  
42. (amended) The lysosomal enzyme [or modified lysosomal enzyme] of claim [39] 61, in which the modified lysosomal enzyme comprises a signal peptide or detectable marker peptide [fused to] at the amino or carboxyl terminal of the modified lysosomal enzyme.

65  
43. (amended) The [lysosomal enzyme or] modified lysosomal enzyme of claim 42, in which the detectable marker peptide comprises SEQ ID NO:10.

69  
44. (amended) The lysosomal enzyme [or modified lysosomal enzyme] of claim 39, in which the transgenic plant is a transgenic tobacco plant.

70  
45. (amended) The lysosomal enzyme [or modified lysosomal enzyme] of any of claims 39, 41 and 44] of claim 39, in which the lysosomal enzyme [or modified lysosomal enzyme] is a human or animal lysosomal enzyme or [modified human lysosomal enzyme].

<sup>72</sup>  
46. (amended) The lysosomal enzyme [or modified lysosomal enzyme] of claim [45] <sup>71</sup>20, in which the [human] lysosomal enzyme [or modified human lysosomal enzyme] is a human glucocerebrosidase or [modified glucocerebrosidase,] human  $\alpha$ -L-iduronidase [or modified  $\alpha$ -L-iduronidase].

<sup>5</sup>  
<sup>2</sup>  
47. (amended) The method according to claim <sup>2</sup>2, which is carried out [in] with the transgenic plant and additionally comprises[, between steps (a) and (b), the] a step of inducing the inducible promoter before or after the transgenic plant is harvested, which inducing step is carried out before recovering the lysosomal enzyme from the cell, tissue or organ of the transgenic plant.

<sup>62</sup>  
<sup>62</sup>  
48. (amended) The lysosomal enzyme [or modified lysosomal enzyme] of claim <sup>60</sup>40, which process is carried out [in] with the transgenic plant and additionally comprises[, between steps (a) and (b), the] a step of inducing the inducible promoter before or after the transgenic plant is harvested, which inducing step is carried out before recovering the lysosomal enzyme from the cell, tissue or organ of the transgenic plant.

<sup>35</sup>  
49. (twice amended) A plant transfection vector comprising the recombinant expression construct of claim <sup>10</sup>10, <sup>11</sup>11, <sup>14</sup>14, <sup>16</sup>16, <sup>17</sup>17, <sup>55</sup>55, <sup>57</sup>57 or <sup>72</sup>72.

C  
Please add the following new claims.

-- <sup>13</sup>  
51. (new) The method according to claim 1, in which the lysosomal enzyme is a modified lysosomal enzyme which is enzymatically active and comprises:

- (a) an enzymatically-active fragment of a human or animal lysosomal enzyme;
- (b) the human or animal lysosomal enzyme or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the human or animal lysosomal enzyme or (a); or
- (c) the human or animal lysosomal enzyme or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

<sup>11</sup>  
52. (new) The method according to claim <sup>6</sup>51, in which the modified lysosomal enzyme comprises:

- (a) an enzymatically-active fragment of an  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase or sialidase;
- (b) the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a); or
- (c) the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

B13 contd.  
53. (new) The method according to claim 52, in which the modified lysosomal enzyme comprises:

- (a) an enzymatically-active fragment of a human glucocerebrosidase or human  $\alpha$ -L-iduronidase enzyme;
- (b) the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a); or
- (c) the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

54. (new) The method according to claim 1, in which the organ is leaf, stem, root, flower, fruit or seed.

55. (new) The recombinant expression construct of claim 10, in which the lysosomal enzyme is a modified lysosomal enzyme which is enzymatically active and comprises:

- (a) an enzymatically-active fragment of a human or animal lysosomal enzyme;

- (b) the human or animal lysosomal enzyme or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the human or animal lysosomal enzyme or (a); or
- (c) the human or animal lysosomal enzyme or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

<sup>26</sup>56. (new) The recombinant expression construct of claim <sup>23</sup>55, in which the modified lysosomal enzyme comprises:

- (a) an enzymatically-active fragment of an  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase or sialidase;
- (b) the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a); or
- (c) the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

<sup>27</sup>57. (new) The recombinant expression construct of claim <sup>26</sup>56, in which the modified lysosomal enzyme comprises:

- (a) an enzymatically-active fragment of a human glucocerebrosidase or human  $\alpha$ -L-iduronidase enzyme;
- (b) the human glucocerebrosidase or human  $\alpha$ -L-iduronidase or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a); or
- (c) the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

44  
58. (new) The transgenic plant or plant cell of claim 25<sup>40</sup>, in which the lysosomal enzyme which is a modified lysosomal enzyme which is enzymatically active and which comprises:

- (a) an enzymatically-active fragment of a human or animal lysosomal enzyme;
- (b) the human or animal lysosomal enzyme or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the human or animal lysosomal enzyme or (a); or
- (c) the human or animal lysosomal enzyme or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

47  
59. (new) The transgenic plant or plant cell of claim 58<sup>44</sup>, in which the modified lysosomal enzyme comprises:

- B 13 and.
- (a) an enzymatically-active fragment of an  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase or sialidase;
  - (b) the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a); or
  - (c) the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

46  
60. (new) The transgenic plant or plant cell of claim 59<sup>47</sup>, in which the modified lysosomal enzyme comprises:

- (a) an enzymatically-active fragment of a human glucocerebrosidase or human  $\alpha$ -L-iduronidase enzyme;
- (b) the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a); or



- (c) the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

~~63~~ 61. (new) The lysosomal enzyme of claim ~~39~~ <sup>59</sup>, which is a modified lysosomal enzyme which is enzymatically active and comprises:

- (a) an enzymatically-active fragment of a human or animal lysosomal enzyme;
- (b) the human or animal lysosomal enzyme or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the human or animal lysosomal enzyme or (a); or
- (c) the human or animal lysosomal enzyme or (a) having one or more naturally-occurring amino acid, additions, deletions or substitutions.

~~66~~ 62. (new) The lysosomal enzyme of claim ~~61~~ <sup>63</sup>, in which the modified lysosomal enzyme comprises:

- P13 Contd.*
- (a) an enzymatically-active fragment of an  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase or sialidase;
  - (b) the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a); or
  - (c) the  $\alpha$ -N-acetylgalactosaminidase, acid lipase,  $\alpha$ -galactosidase, glucocerebrosidase,  $\alpha$ -L-iduronidase, iduronate sulfatase,  $\alpha$ -mannosidase, sialidase or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

~~67~~ 63. (new) The lysosomal enzyme of claim ~~62~~ <sup>66</sup>, in which the modified lysosomal enzyme comprises:

- (a) an enzymatically-active fragment of a human glucocerebrosidase or human  $\alpha$ -L-iduronidase enzyme;

- (b) the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a) having one or more amino acid residues added to the amino or carboxyl terminus of the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a); or
- (c) the human glucocerebrosidase, human  $\alpha$ -L-iduronidase or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions.

<sup>77</sup>64. (new) The lysosomal enzyme of claim <sup>59</sup>39, in which the organ is leaf, stem, root, flower, fruit or seed.

<sup>36</sup>65. (new) A plasmid comprising the recombinant expression construct of claim <sup>19</sup>10, <sup>20</sup>11, <sup>24</sup>14, <sup>29</sup>16, <sup>31</sup>17, <sup>54</sup>or <sup>55</sup>35, <sup>57</sup>59, <sup>61</sup>63, <sup>65</sup>67, <sup>69</sup>71, <sup>73</sup>75, <sup>77</sup>79, <sup>81</sup>83, <sup>85</sup>87, <sup>89</sup>91, <sup>93</sup>95, <sup>97</sup>99, <sup>101</sup>103, <sup>105</sup>107, <sup>109</sup>111, <sup>113</sup>115, <sup>117</sup>119, <sup>121</sup>123, <sup>125</sup>127, <sup>129</sup>131, <sup>133</sup>135, <sup>137</sup>139, <sup>141</sup>143, <sup>145</sup>147, <sup>149</sup>151, <sup>153</sup>155, <sup>157</sup>159, <sup>161</sup>163, <sup>165</sup>167, <sup>169</sup>171, <sup>173</sup>175, <sup>177</sup>179, <sup>181</sup>183, <sup>185</sup>187, <sup>189</sup>191, <sup>193</sup>195, <sup>197</sup>199, <sup>201</sup>203, <sup>205</sup>207, <sup>209</sup>211, <sup>213</sup>215, <sup>217</sup>219, <sup>221</sup>223, <sup>225</sup>227, <sup>229</sup>231, <sup>233</sup>235, <sup>237</sup>239, <sup>241</sup>243, <sup>245</sup>247, <sup>249</sup>251, <sup>253</sup>255, <sup>257</sup>259, <sup>261</sup>263, <sup>265</sup>267, <sup>269</sup>271, <sup>273</sup>275, <sup>277</sup>279, <sup>281</sup>283, <sup>285</sup>287, <sup>289</sup>291, <sup>293</sup>295, <sup>297</sup>299, <sup>301</sup>303, <sup>305</sup>307, <sup>309</sup>311, <sup>313</sup>315, <sup>317</sup>319, <sup>321</sup>323, <sup>325</sup>327, <sup>329</sup>331, <sup>333</sup>335, <sup>337</sup>339, <sup>341</sup>343, <sup>345</sup>347, <sup>349</sup>351, <sup>353</sup>355, <sup>357</sup>359, <sup>361</sup>363, <sup>365</sup>367, <sup>369</sup>371, <sup>373</sup>375, <sup>377</sup>379, <sup>381</sup>383, <sup>385</sup>387, <sup>389</sup>391, <sup>393</sup>395, <sup>397</sup>399, <sup>401</sup>403, <sup>405</sup>407, <sup>409</sup>411, <sup>413</sup>415, <sup>417</sup>419, <sup>421</sup>423, <sup>425</sup>427, <sup>429</sup>431, <sup>433</sup>435, <sup>437</sup>439, <sup>441</sup>443, <sup>445</sup>447, <sup>449</sup>451, <sup>453</sup>455, <sup>457</sup>459, <sup>461</sup>463, <sup>465</sup>467, <sup>469</sup>471, <sup>473</sup>475, <sup>477</sup>479, <sup>481</sup>483, <sup>485</sup>487, <sup>489</sup>491, <sup>493</sup>495, <sup>497</sup>499, <sup>501</sup>503, <sup>505</sup>507, <sup>509</sup>511, <sup>513</sup>515, <sup>517</sup>519, <sup>521</sup>523, <sup>525</sup>527, <sup>529</sup>531, <sup>533</sup>535, <sup>537</sup>539, <sup>541</sup>543, <sup>545</sup>547, <sup>549</sup>551, <sup>553</sup>555, <sup>557</sup>559, <sup>561</sup>563, <sup>565</sup>567, <sup>569</sup>571, <sup>573</sup>575, <sup>577</sup>579, <sup>581</sup>583, <sup>585</sup>587, <sup>589</sup>591, <sup>593</sup>595, <sup>597</sup>599, <sup>601</sup>603, <sup>605</sup>607, <sup>609</sup>611, <sup>613</sup>615, <sup>617</sup>619, <sup>621</sup>623, <sup>625</sup>627, <sup>629</sup>631, <sup>633</sup>635, <sup>637</sup>639, <sup>641</sup>643, <sup>645</sup>647, <sup>649</sup>651, <sup>653</sup>655, <sup>657</sup>659, <sup>661</sup>663, <sup>665</sup>667, <sup>669</sup>671, <sup>673</sup>675, <sup>677</sup>679, <sup>681</sup>683, <sup>685</sup>687, <sup>689</sup>691, <sup>693</sup>695, <sup>697</sup>699, <sup>701</sup>703, <sup>705</sup>707, <sup>709</sup>711, <sup>713</sup>715, <sup>717</sup>719, <sup>721</sup>723, <sup>725</sup>727, <sup>729</sup>731, <sup>733</sup>735, <sup>737</sup>739, <sup>741</sup>743, <sup>745</sup>747, <sup>749</sup>751, <sup>753</sup>755, <sup>757</sup>759, <sup>761</sup>763, <sup>765</sup>767, <sup>769</sup>771, <sup>773</sup>775, <sup>777</sup>779, <sup>781</sup>783, <sup>785</sup>787, <sup>789</sup>791, <sup>793</sup>795, <sup>797</sup>799, <sup>801</sup>803, <sup>805</sup>807, <sup>809</sup>811, <sup>813</sup>815, <sup>817</sup>819, <sup>821</sup>823, <sup>825</sup>827, <sup>829</sup>831, <sup>833</sup>835, <sup>837</sup>839, <sup>841</sup>843, <sup>845</sup>847, <sup>849</sup>851, <sup>853</sup>855, <sup>857</sup>859, <sup>861</sup>863, <sup>865</sup>867, <sup>869</sup>871, <sup>873</sup>875, <sup>877</sup>879, <sup>881</sup>883, <sup>885</sup>887, <sup>889</sup>891, <sup>893</sup>895, <sup>897</sup>899, <sup>901</sup>903, <sup>905</sup>907, <sup>909</sup>911, <sup>913</sup>915, <sup>917</sup>919, <sup>921</sup>923, <sup>925</sup>927, <sup>929</sup>931, <sup>933</sup>935, <sup>937</sup>939, <sup>941</sup>943, <sup>945</sup>947, <sup>949</sup>951, <sup>953</sup>955, <sup>957</sup>959, <sup>961</sup>963, <sup>965</sup>967, <sup>969</sup>971, <sup>973</sup>975, <sup>977</sup>979, <sup>981</sup>983, <sup>985</sup>987, <sup>989</sup>991, <sup>993</sup>995, <sup>997</sup>999, <sup>1001</sup>1003, <sup>1005</sup>1007, <sup>1009</sup>1011, <sup>1013</sup>1015, <sup>1017</sup>1019, <sup>1021</sup>1023, <sup>1025</sup>1027, <sup>1029</sup>1031, <sup>1033</sup>1035, <sup>1037</sup>1039, <sup>1041</sup>1043, <sup>1045</sup>1047, <sup>1049</sup>1051, <sup>1053</sup>1055, <sup>1057</sup>1059, <sup>1061</sup>1063, <sup>1065</sup>1067, <sup>1069</sup>1071, <sup>1073</sup>1075, <sup>1077</sup>1079, <sup>1081</sup>1083, <sup>1085</sup>1087, <sup>1089</sup>1091, <sup>1093</sup>1095, <sup>1097</sup>1099, <sup>1101</sup>1103, <sup>1105</sup>1107, <sup>1109</sup>1111, <sup>1113</sup>1115, <sup>1117</sup>1119, <sup>1121</sup>1123, <sup>1125</sup>1127, <sup>1129</sup>1131, <sup>1133</sup>1135, <sup>1137</sup>1139, <sup>1141</sup>1143, <sup>1145</sup>1147, <sup>1149</sup>1151, <sup>1153</sup>1155, <sup>1157</sup>1159, <sup>1161</sup>1163, <sup>1165</sup>1167, <sup>1169</sup>1171, <sup>1173</sup>1175, <sup>1177</sup>1179, <sup>1181</sup>1183, <sup>1185</sup>1187, <sup>1189</sup>1191, <sup>1193</sup>1195, <sup>1197</sup>1199, <sup>1201</sup>1203, <sup>1205</sup>1207, <sup>1209</sup>1211, <sup>1213</sup>1215, <sup>1217</sup>1219, <sup>1221</sup>1223, <sup>1225</sup>1227, <sup>1229</sup>1231, <sup>1233</sup>1235, <sup>1237</sup>1239, <sup>1241</sup>1243, <sup>1245</sup>1247, <sup>1249</sup>1251, <sup>1253</sup>1255, <sup>1257</sup>1259, <sup>1261</sup>1263, <sup>1265</sup>1267, <sup>1269</sup>1271, <sup>1273</sup>1275, <sup>1277</sup>1279, <sup>1281</sup>1283, <sup>1285</sup>1287, <sup>1289</sup>1291, <sup>1293</sup>1295, <sup>1297</sup>1299, <sup>1301</sup>1303, <sup>1305</sup>1307, <sup>1309</sup>1311, <sup>1313</sup>1315, <sup>1317</sup>1319, <sup>1321</sup>1323, <sup>1325</sup>1327, <sup>1329</sup>1331, <sup>1333</sup>1335, <sup>1337</sup>1339, <sup>1341</sup>1343, <sup>1345</sup>1347, <sup>1349</sup>1351, <sup>1353</sup>1355, <sup>1357</sup>1359, <sup>1361</sup>1363, <sup>1365</sup>1367, <sup>1369</sup>1371, <sup>1373</sup>1375, <sup>1377</sup>1379, <sup>1381</sup>1383, <sup>1385</sup>1387, <sup>1389</sup>1391, <sup>1393</sup>1395, <sup>1397</sup>1399, <sup>1401</sup>1403, <sup>1405</sup>1407, <sup>1409</sup>1411, <sup>1413</sup>1415, <sup>1417</sup>1419, <sup>1421</sup>1423, <sup>1425</sup>1427, <sup>1429</sup>1431, <sup>1433</sup>1435, <sup>1437</sup>1439, <sup>1441</sup>1443, <sup>1445</sup>1447, <sup>1449</sup>1451, <sup>1453</sup>1455, <sup>1457</sup>1459, <sup>1461</sup>1463, <sup>1465</sup>1467, <sup>1469</sup>1471, <sup>1473</sup>1475, <sup>1477</sup>1479, <sup>1481</sup>1483, <sup>1485</sup>1487, <sup>1489</sup>1491, <sup>1493</sup>1495, <sup>1497</sup>1499, <sup>1501</sup>1503, <sup>1505</sup>1507, <sup>1509</sup>1511, <sup>1513</sup>1515, <sup>1517</sup>1519, <sup>1521</sup>1523, <sup>1525</sup>1527, <sup>1529</sup>1531, <sup>1533</sup>1535, <sup>1537</sup>1539, <sup>1541</sup>1543, <sup>1545</sup>1547, <sup>1549</sup>1551, <sup>1553</sup>1555, <sup>1557</sup>1559, <sup>1561</sup>1563, <sup>1565</sup>1567, <sup>1569</sup>1571, <sup>1573</sup>1575, <sup>1577</sup>1579, <sup>1581</sup>1583, <sup>1585</sup>1587, <sup>1589</sup>1591, <sup>1593</sup>1595, <sup>1597</sup>1599, <sup>1601</sup>1603, <sup>1605</sup>1607, <sup>1609</sup>1611, <sup>1613</sup>1615, <sup>1617</sup>1619, <sup>1621</sup>1623, <sup>1625</sup>1627, <sup>1629</sup>1631, <sup>1633</sup>1635, <sup>1637</sup>1639, <sup>1641</sup>1643, <sup>1645</sup>1647, <sup>1649</sup>1651, <sup>1653</sup>1655, <sup>1657</sup>1659, <sup>1661</sup>1663, <sup>1665</sup>1667, <sup>1669</sup>1671, <sup>1673</sup>1675, <sup>1677</sup>1679, <sup>1681</sup>1683, <sup>1685</sup>1687, <sup>1689</sup>1691, <sup>1693</sup>1695, <sup>1697</sup>1699, <sup>1701</sup>1703, <sup>1705</sup>1707, <sup>1709</sup>1711, <sup>1713</sup>1715, <sup>1717</sup>1719, <sup>1721</sup>1723, <sup>1725</sup>1727, <sup>1729</sup>1731, <sup>1733</sup>1735, <sup>1737</sup>1739, <sup>1741</sup>1743, <sup>1745</sup>1747, <sup>1749</sup>1751, <sup>1753</sup>1755, <sup>1757</sup>1759, <sup>1761</sup>1763, <sup>1765</sup>1767, <sup>1769</sup>1771, <sup>1773</sup>1775, <sup>1777</sup>1779, <sup>1781</sup>1783, <sup>1785</sup>1787, <sup>1789</sup>1791, <sup>1793</sup>1795, <sup>1797</sup>1799, <sup>1801</sup>1803, <sup>1805</sup>1807, <sup>1809</sup>1811, <sup>1813</sup>1815, <sup>1817</sup>1819, <sup>1821</sup>1823, <sup>1825</sup>1827, <sup>1829</sup>1831, <sup>1833</sup>1835, <sup>1837</sup>1839, <sup>1841</sup>1843, <sup>1845</sup>1847, <sup>1849</sup>1851, <sup>1853</sup>1855, <sup>1857</sup>1859, <sup>1861</sup>1863, <sup>1865</sup>1867, <sup>1869</sup>1871, <sup>1873</sup>1875, <sup>1877</sup>1879, <sup>1881</sup>1883, <sup>1885</sup>1887, <sup>1889</sup>1891, <sup>1893</sup>1895, <sup>1897</sup>1899, <sup>1901</sup>1903, <sup>1905</sup>1907, <sup>1909</sup>1911, <sup>1913</sup>1915, <sup>1917</sup>1919, <sup>1921</sup>1923, <sup>1925</sup>1927, <sup>1929</sup>1931, <sup>1933</sup>1935, <sup>1937</sup>1939, <sup>1941</sup>1943, <sup>1945</sup>1947, <sup>1949</sup>1951, <sup>1953</sup>1955, <sup>1957</sup>1959, <sup>1961</sup>1963, <sup>1965</sup>1967, <sup>1969</sup>1971, <sup>1973</sup>1975, <sup>1977</sup>1979, <sup>1981</sup>1983, <sup>1985</sup>1987, <sup>1989</sup>1991, <sup>1993</sup>1995, <sup>1997</sup>1999, <sup>2001</sup>2003, <sup>2005</sup>2007, <sup>2009</sup>2011, <sup>2013</sup>2015, <sup>2017</sup>2019, <sup>2021</sup>2023, <sup>2025</sup>2027, <sup>2029</sup>2031, <sup>2033</sup>2035, <sup>2037</sup>2039, <sup>2041</sup>2043, <sup>2045</sup>2047, <sup>2049</sup>2051, <sup>2053</sup>2055, <sup>2057</sup>2059, <sup>2061</sup>2063, <sup>2065</sup>2067, <sup>2069</sup>2071, <sup>2073</sup>2075, <sup>2077</sup>2079, <sup>2081</sup>2083, <sup>2085</sup>2087, <sup>2089</sup>2091, <sup>2093</sup>2095, <sup>2097</sup>2099, <sup>2101</sup>2103, <sup>2105</sup>2107, <sup>2109</sup>2111, <sup>2113</sup>2115, <sup>2117</sup>2119, <sup>2121</sup>2123, <sup>2125</sup>2127, <sup>2129</sup>2131, <sup>2133</sup>2135, <sup>2137</sup>2139, <sup>2141</sup>2143, <sup>2145</sup>2147, <sup>2149</sup>2151, <sup>2153</sup>2155, <sup>2157</sup>2159, <sup>2161</sup>2163, <sup>2165</sup>2167, <sup>2169</sup>2171, <sup>2173</sup>2175, <sup>2177</sup>2179, <sup>2181</sup>2183, <sup>2185</sup>2187, <sup>2189</sup>2191, <sup>2193</sup>2195, <sup>2197</sup>2199, <sup>2201</sup>2203, <sup>2205</sup>2207, <sup>2209</sup>2211, <sup>2213</sup>2215, <sup>2217</sup>2219, <sup>2221</sup>2223, <sup>2225</sup>2227, <sup>2229</sup>2231, <sup>2233</sup>2235, <sup>2237</sup>2239, <sup>2241</sup>2243, <sup>2245</sup>2247, <sup>2249</sup>2251, <sup>2253</sup>2255, <sup>2257</sup>2259, <sup>2261</sup>2263, <sup>2265</sup>2267, <sup>2269</sup>2271, <sup>2273</sup>2275, <sup>2277</sup>2279, <sup>2281</sup>2283, <sup>2285</sup>2287, <sup>2289</sup>2291, <sup>2293</sup>2295, <sup>2297</sup>2299, <sup>2301</sup>2303, <sup>2305</sup>2307, <sup>2309</sup>2311, <sup>2313</sup>2315, <sup>2317</sup>2319, <sup>2321</sup>2323, <sup>2325</sup>2327, <sup>2329</sup>2331, <sup>2333</sup>2335, <sup>2337</sup>2339, <sup>2341</sup>2343, <sup>2345</sup>2347, <sup>2349</sup>2351, <sup>2353</sup>2355, <sup>2357</sup>2359, <sup>2361</sup>2363, <sup>2365</sup>2367, <sup>2369</sup>2371, <sup>2373</sup>2375, <sup>2377</sup>2379, <sup>2381</sup>2383, <sup>2385</sup>2387, <sup>2389</sup>2391, <sup>2393</sup>2395, <sup>2397</sup>2399, <sup>2401</sup>2403, <sup>2405</sup>2407, <sup>2409</sup>2411, <sup>2413</sup>2415, <sup>2417</sup>2419, <sup>2421</sup>2423, <sup>2425</sup>2427, <sup>2429</sup>2431, <sup>2433</sup>2435, <sup>2437</sup>2439, <sup>2441</sup>2443, <sup>2445</sup>2447, <sup>2449</sup>2451, <sup>2453</sup>2455, <sup>2457</sup>2459, <sup>2461</sup>2463, <sup>2465</sup>2467, <sup>2469</sup>2471, <sup>2473</sup>2475, <sup>2477</sup>2479, <sup>2481</sup>2483, <sup>2485</sup>2487, <sup>2489</sup>2491, <sup>2493</sup>2495, <sup>2497</sup>2499, <sup>2501</sup>2503, <sup>2505</sup>2507, <sup>2509</sup>2511, <sup>2513</sup>2515, <sup>2517</sup>2519, <sup>2521</sup>2523, <sup>2525</sup>2527, <sup>2529</sup>2531, <sup>2533</sup>2535, <sup>2537</sup>2539, <sup>2541</sup>2543, <sup>2545</sup>2547, <sup>2549</sup>2551, <sup>2553</sup>2555, <sup>2557</sup>2559, <sup>2561</sup>2563, <sup>2565</sup>2567, <sup>2569</sup>2571, <sup>2573</sup>2575, <sup>2577</sup>2579, <sup>2581</sup>2583, <sup>2585</sup>2587, <sup>2589</sup>2591, <sup>2593</sup>2595, <sup>2597</sup>2599, <sup>2601</sup>2603, <sup>2605</sup>2607, <sup>2609</sup>2611, <sup>2613</sup>2615, <sup>2617</sup>2619, <sup>2621</sup>2623, <sup>2625</sup>2627, <sup>2629</sup>2631, <sup>2633</sup>2635, <sup>2637</sup>2639, <sup>2641</sup>2643, <sup>2645</sup>2647, <sup>2649</sup>2651, <sup>2653</sup>2655, <sup>2657</sup>2659, <sup>2661</sup>2663, <sup>2665</sup>2667, <sup>2669</sup>2671, <sup>2673</sup>2675, <sup>2677</sup>2679, <sup>2681</sup>2683, <sup>2685</sup>2687, <sup>2689</sup>2691, <sup>2693</sup>2695, <sup>2697</sup>2699, <sup>2701</sup>2703, <sup>2705</sup>2707, <sup>2709</sup>2711, <sup>2713</sup>2715, <sup>2717</sup>2719, <sup>2721</sup>2723, <sup>2725</sup>2727, <sup>2729</sup>2731, <sup>2733</sup>2735, <sup>2737</sup>2739, <sup>2741</sup>2743, <sup>2745</sup>2747, <sup>2749</sup>2751, <sup>2753</sup>2755, <sup>2757</sup>2759, <sup>2761</sup>2763, <sup>2765</sup>2767, <sup>2769</sup>2771, <sup>2773</sup>2775, <sup>2777</sup>2779, <sup>2781</sup>2783, <sup>2785</sup>2787, <sup>2789</sup>2791, <sup>2793</sup>2795, <sup>2797</sup>2799, <sup>2801</sup>2803, <sup>2805</sup>2807, <sup>2809</sup>2811, <sup>2813</sup>2815, <sup>2817</sup>2819, <sup>2821</sup>2823, <sup>2825</sup>2827, <sup>2829</sup>2831, <sup>2833</sup>2835, <sup>2837</sup>2839, <sup>2841</sup>2843, <sup>2845</sup>2847, <sup>2849</sup>2851, <sup>2853</sup>2855, <sup>2857</sup>2859, <sup>2861</sup>2863, <sup>2865</sup>2867, <sup>2869</sup>2871, <sup>2873</sup>2875, <sup>2877</sup>2879, <sup>2881</sup>2883, <sup>2885</sup>2887, <sup>2889</sup>2891, <sup>2893</sup>2895, <sup>2897</sup>2899, <sup>2901</sup>2903, <sup>2905</sup>2907, <sup>2909</sup>2911, <sup>2913</sup>2915, <sup>2917</sup>2919, <sup>2921</sup>2923, <sup>2925</sup>2927, <sup>2929</sup>2931, <sup>2933</sup>2935, <sup>2937</sup>2939, <sup>2941</sup>2943, <sup>2945</sup>2947, <sup>2949</sup>2951, <sup>2953</sup>2955, <sup>2957</sup>2959, <sup>2961</sup>2963, <sup>2965</sup>2967, <sup>2969</sup>2971, <sup>2973</sup>2975, <sup>2977</sup>2979, <sup>2981</sup>2983, <sup>2985</sup>2987, <sup>2989</sup>2991, <sup>2993</sup>2995, <sup>2997</sup>2999, <sup>3001</sup>3003, <sup>3005</sup>3007, <sup>3009</sup>3011, <sup>3013</sup>3015, <sup>3017</sup>3019, <sup>3021</sup>3023, <sup>3025</sup>3027, <sup>3029</sup>3031, <sup>3033</sup>3035, <sup>3037</sup>3039, <sup>3041</sup>3043, <sup>3045</sup>3047, <sup>3049</sup>3051, <sup>3053</sup>3055, <sup>3057</sup>3059, <sup>3061</sup>3063, <sup>3065</sup>3067, <sup>3069</sup>3071, <sup>3073</sup>3075, <sup>3077</sup>3079, <sup>3081</sup>3083, <sup>3085</sup>3087, <sup>3089</sup>3091, <sup>3093</sup>3095, <sup>3097</sup>3099, <sup>3101</sup>3103, <sup>3105</sup>3107, <sup>3109</sup>3111, <sup>3113</sup>3115, <sup>3117</sup>3119, <sup>3121</sup>3123, <sup>3125</sup>3127, <sup>3129</sup>3131, <sup>3133</sup>3135, <sup>3137</sup>3139, <sup>3141</sup>3143, <sup>3145</sup>3147, <sup>3149</sup>3151, <sup>3153</sup>3155, <sup>3157</sup>3159, <sup>3161</sup>3163, <sup>3165</sup>3167, <sup>3169</sup>3171, <sup>3173</sup>3175, <sup>3177</sup>3179, <sup>3181</sup>3183, <sup>3185</sup>3187, <sup>3189</sup>3191, <sup>3193</sup>3195, <sup>3197</sup>3199, <sup>3201</sup>3203, <sup>3205</sup>3207, <sup>3209</sup>3211, <sup>3213</sup>3215, <sup>3217</sup>3219, <sup>3221</sup>3223, <sup>3225</sup>3227, <sup>3229</sup>3231, <sup>3233</sup>3235, <sup>3237</sup>3239, <sup>3241</sup>3243, <sup>3245</sup>3247, <sup>3249</sup>3251, <sup>3253</sup>3255, <sup>3257</sup>3259, <sup>3261</sup>3263, <sup>3265</sup>3267, <sup>3269</sup>3271, <sup>3273</sup>3275, <sup>3277</sup>3279, <sup>3281</sup>3283, <sup>3285</sup>3287, <sup>3289</sup>3291, <sup>3293</sup>3295, <sup>3297</sup>3299, <sup>3301</sup>3303, <sup>3305</sup>3307, <sup>3309</sup>3311, <sup>3313</sup>3315, <sup>3317</sup>3319, <sup>3321</sup>3323, <sup>3325</sup>3327, <sup>3329</sup>3331, <sup>3333</sup>3335, <sup>3337</sup>3339, <sup>3341</sup>3343, <sup>3345</sup>3347, <sup>3349</sup>3351, <sup>3353</sup>3355, <sup>3357</sup>3359, <sup>3361</sup>3363, <sup>3365</sup>3367, <sup>3369</sup>3371, <sup>3373</sup>3375, <sup>3377</sup>3379, <sup>3381</sup>3383, <sup>3385</sup>

- (I) (a) the enzymatically-active fragment of the human or animal lysosomal enzyme,  
(b) the human or animal lysosomal enzyme, or  
(c) the human or animal lysosomal enzyme or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions, and

(II) a cleavable linker fused to the amino or carboxyl terminus of (I);  
and the method comprises:

- (i) recovering the fusion protein from the transgenic plant cell, or the cell, tissue or organ of the transgenic plant;  
(ii) treating the fusion protein with a substance that cleaves the cleavable linker so that (I) is separated from the cleavable linker and any sequence attached thereto; and  
(iii) recovering the separated (I).

<sup>28</sup>  
~~72~~ (new) The expression construct of claim ~~55~~<sup>23</sup>, in which the modified lysosomal enzyme is a fusion protein comprising

- (I) (a) the enzymatically-active fragment of the human or animal lysosomal enzyme,  
(b) the human or animal lysosomal enzyme, or  
(c) the human or animal lysosomal enzyme or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions, and  
(II) a cleavable linker fused to the amino or carboxyl terminus of (I).

<sup>49</sup>  
~~73~~ (new) The transgenic plant or plant cell of claim ~~58~~<sup>44</sup>, in which the modified lysosomal enzyme is a fusion protein comprising:

- (I) (a) the enzymatically-active fragment of the human or animal lysosomal enzyme,  
(b) the human or animal lysosomal enzyme, or  
(c) the human or animal lysosomal enzyme or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions, and

(II) a cleavable linker fused to the amino or carboxyl terminus of (I).

<sup>68</sup>  
~~74~~. (new) The lysosomal enzyme of claim <sup>63</sup>~~61~~, in which the modified lysosomal enzyme is a fusion protein comprising:

- (I) (a) the enzymatically-active fragment of the human or animal lysosomal enzyme,  
(b) the human or animal lysosomal enzyme, or  
(c) the human or animal lysosomal enzyme or (a) having one or more naturally-occurring amino acid additions, deletions or substitutions, and

(II) a cleavable linker fused to the amino or carboxyl terminus of (I).

<sup>8</sup>  
~~75~~. (new) The method according to claim <sup>7</sup>~~5~~, in which the modified lysosomal enzyme is recovered from (i) the transgenic plant cell or (ii) the cell, tissue or organ of the transgenic plant by reacting with an antibody that binds the detectable marker peptide.

<sup>9</sup>  
~~76~~. (new) The method according to claim <sup>7</sup>~~5~~, in which the antibody is a monoclonal antibody.--

IN THE SEQUENCE LISTING:

Please correct the Sequence Listing by deleting the present Sequence Listing and replace with the second substitute Sequence Listing (10 pages) submitted concurrently herewith.

REMARKS

The drawing of Figure 11 has been amended to correct several inadvertent errors in the MeGA promoter sequence shown. Applicants respectfully invite the Examiner's attention to the Declaration by Karen K. Oishi submitted concurrently herewith. The Declaration supports the correction of Figure 11. In the Declaration, Dr. Oishi, who is a co-inventor of the present application, states that her careful review of sequence data of the MeGA promoter indicates that the MeGA promoter sequence shown in Figure 11 originally filed with the application contains several inadvertent errors (see